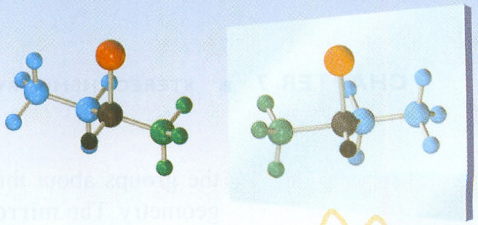
VISIT…



Stereochemistry II

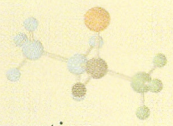
CHIRAL MOLECULES

CHAPTER 7

THIS CHAPTER introduces a new type of stereoisomer, the most subtle that we will encounter. This type of stereoisomer arises because of the tetrahedral geometry of singly bonded carbon. After this stereoisomerism is described, a discussion of how to recognize when these stereoisomers occur is presented. Next, a method to designate the configuration of these stereoisomers is described. After a discussion of when their properties differ, more complex examples are described. Finally, how they are prepared and how they are separated are considered.

Although you are probably getting better at seeing the three-dimensional shapes of molecules when viewing two-dimensional representations, it is still worthwhile to construct models to help you understand the material in this chapter. And remember to take advantage of the online computer models that are available for the molecules discussed in this chapter.

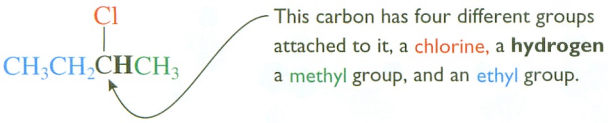
MASTERING ORGANIC CHEMISTRY



- Identifying Chiral Compounds and Locating Chirality Centers
- Locating Symmetry Planes
- Designating the Configuration of Chirality Centers
- Recognizing When Enantiomers Have Different Properties
- Understanding Optical Activity
- Recognizing Meso Stereoisomers
- Understanding How to Separate Enantiomers
- Using Fischer Projections
- Identifying Other Types of Chiral Molecules

7.1 CHIRAL MOLECULES

Even some fairly simple molecules, such as 2-chlorobutane, exhibit this new type of isomerism just mentioned. The special feature of 2-chlorobutane that causes it to exhibit this type of stereoisomerism is that one of its carbons has four different groups attached to it.


Cl
CH3CH2CHCH3
This carbon has four different groups attached to it, a chlorine, a hydrogen a methyl group, and an ethyl group.

To see this new type of isomer, we must carefully examine the arrangement of the four groups around this carbon. The following structure shows the arrangement of

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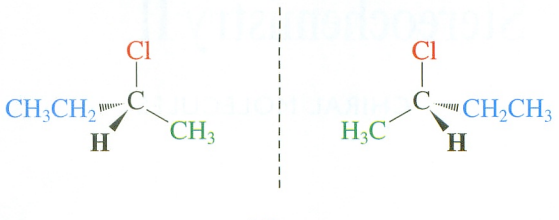
the groups about this carbon, which is, of course, sp^3 hybridized and has tetrahedral geometry. The **mirror image** of the original structure is also shown.



Careful examination of these two structures shows that they are not identical. This can more easily be seen if the right structure is rotated 180° about the axis of the C—Cl bond:

This is the left structure.

This is the right structure, rotated 180° about the C—Cl bond.

The chlorines and the methyl groups occupy the same positions in these two structures, but the hydrogens and the ethyl groups do not. If one structure is rotated so that the ethyl groups and the hydrogens occupy the same positions, the chlorines and the methyl groups will not occupy the same positions. The two structures cannot be superimposed on one another. No amount of rotating of these structures will ever make them the same—they are **nonsuperimposable mirror images.** The only way to make these two structures identical is to interchange two groups (any two) in one of the structures. Of course, this requires bonds to be broken and does not occur at room temperature. Figure 7.1 shows three-dimensional models of these compounds. Many students have some difficulty seeing that these structures are different and cannot be superimposed by examining drawings. The use of handheld models can be invaluable in helping with this visualization.

MODEL BUILDING PROBLEM 7.1

Build a handheld model of a tetrahedral carbon with four differently colored bonds. Build the mirror image of this model. Show that the models cannot be superimposed; that is, show that you cannot line up all the bonds of the same color. Interchange two bonds on one of the models and determine whether they can be superimposed.

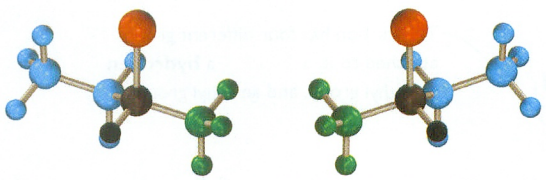


Figure 7.1

STEREOISOMERS OF 2-CHLOROBUTANE.

ORGANIC Chemistry Now™
Click *Molecular Models* to view computer models of most of the molecules discussed in this chapter.

Molecules such as 2-chlorobutane are termed **chiral.** Chiral molecules exist as either of two stereoisomeric structures. These stereoisomers, a pair of nonsuperimposable mirror images, are called **enantiomers.**

It is easier to understand this kind of stereoisomer if we think about some everyday objects that are chiral. One example of a chiral object is a hand. (In fact, the term *chiral* is derived from the Greek word for hand, *kheir*.) A left hand and a right hand are enantiomers—they are nonsuperimposable mirror images. Other examples of everyday objects that are chiral are feet, gloves, golf clubs, screws, and handwriting. We say that all of these objects exhibit *handedness*. Objects that are **achiral** (not chiral) include socks, some types of mittens, baseball bats, screwdrivers, blank paper, and pencils.

PROBLEM 7.1

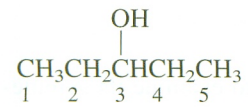
Indicate whether each of these objects is chiral or achiral:

a) Golf ball **b)** Baseball glove
c) Clock **d)** T-shirt
e) Dress shirt **f)** Automobile

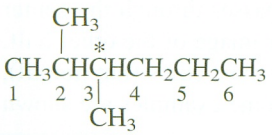
7.2 Recognizing Chiral Molecules

How do we recognize when a molecule is chiral? The most certain method is to build a model of the molecule and then build a model of its mirror image. If the two models are superimposable in any conformation, the molecule is achiral; if they are not, it is chiral. However, this method is tedious and does not provide any understanding of what is the cause of a molecule being chiral. A faster, more instructive method is needed.

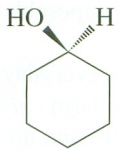
The feature of 2-chlorobutane that makes it chiral is the presence of a carbon attached to four different groups. Such carbons are another type of stereocenter. The currently accepted term to describe such a carbon, or any other tetrahedral atom attached to four different groups, is **chirality center.** (Some older terms that you may encounter are *chiral carbon atom* or *asymmetric carbon atom*.) Any molecule with one chirality center as its only stereocenter is chiral. (As we shall see shortly, many, but not all, molecules with multiple chirality centers are also chiral.) So, another way to identify a chiral molecule is to look for a single chirality center, which requires some practice. It helps to remember that any carbon that is attached to two identical groups (this includes all doubly and triply bonded carbons) is not a chirality center. Consider these examples:



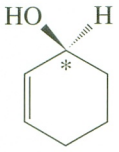
This compound has no chirality center and is not chiral. Carbons 1, 2, 4, and 5 are all bonded to at least two hydrogens. Carbon 3 has one hydrogen, one hydroxy, and two ethyl groups attached to it.



Carbons 1, 4, 5, and 6 are all bonded to two or more hydrogens, so they are not chirality centers. Carbon 2 is bonded to two methyl groups, so it is not a chirality center either. However, carbon 3 is bonded to four different groups (hydrogen, methyl, propyl, isopropyl) and is a chirality center. Because the molecule has one chirality center, it is chiral. Chirality centers are sometimes marked with an asterisk (*).



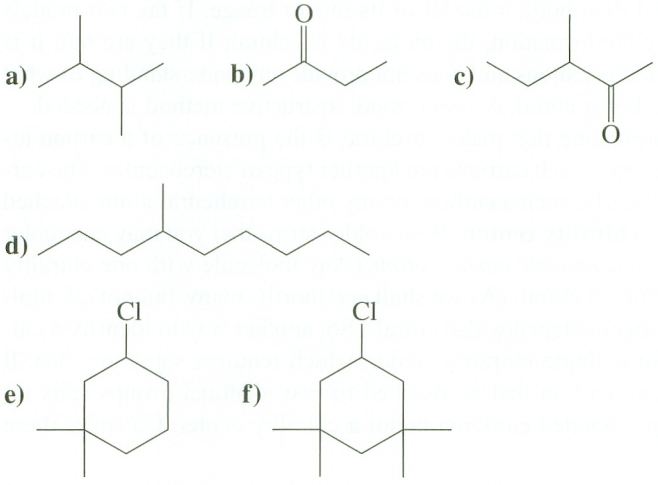
Ring compounds are a little trickier. In this case, all of the carbons except one are bonded to two hydrogens and are not chirality centers. What about the carbon bonded to the hydrogen and the hydroxy group? The other two "groups" that are bonded to this carbon are the carbons of the ring. These groups are identical proceeding around the ring in either direction, so the carbon is not a chirality center and the molecule is not chiral. Note that it is not necessary to consider conformations in this analysis of chirality.



In contrast to the preceding example, the carbon bonded to the hydrogen and the hydroxy group is a chirality center in this molecule. In proceeding around the ring in one direction, the first carbon encountered is part of a double bond; in the other direction, it is not. In ring systems, one must step around the ring in both directions, comparing one carbon at a time. If a difference is found at any point, then the "groups" are different.

PROBLEM 7.2

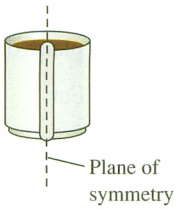
Determine whether each of these molecules is chiral. For those that are chiral, put an asterisk at the chirality center.



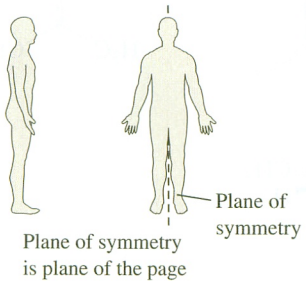
A final way to determine whether a molecule is chiral is to examine its symmetry. Although an object can have several different kinds of symmetry, the only kind that will be of concern to us is called a **plane of symmetry** or a **mirror plane.** An object has a plane of symmetry if an imaginary plane that passes through the center of the object divides the object so that one half is the mirror image of the other half. Any molecule that has a plane of symmetry is not chiral. In most cases (but not all), if no plane of symmetry is present, the molecule is chiral. Some examples are shown in Figure 7.2.

Figure 7.2

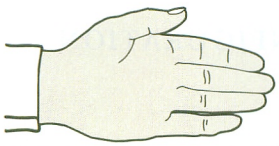
SOME OBJECTS AND MOLECULES WITH AND WITHOUT A PLANE OF SYMMETRY.



A cup has a plane of symmetry that passes vertically through it and bisects the handle. It is not chiral.

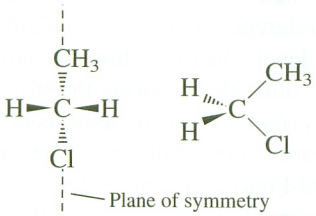


Two views of the plane of symmetry present in an idealized human figure. Although the figure has chiral parts (such as hands), they are arranged in pairs so that one chiral part mirrors the other. Overall, a human is not chiral.



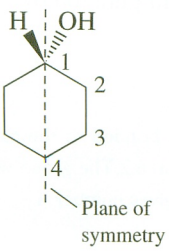
A hand has no plane of symmetry and is chiral.

Chloroethane



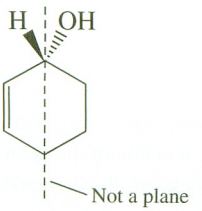
Chloroethanol has a plane of symmetry that passes through the two carbons and the chlorine. The plane is perpendicular to the page in the model and left drawing and is the plane of the page in the right drawing. The hydrogens mirror each other. This compound is not chiral.

Cyclohexanol



Cyclohexanol is achiral because it has no chirality center. The same conclusion can be reached by noting that it has a plane of symmetry that is perpendicular to the page and that passes through carbon 1, the hydrogen and hydroxy group attached to it, and carbon 4. One side of the ring mirrors the other side.

2-Cyclohexenol

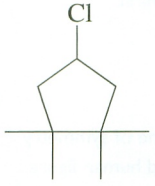


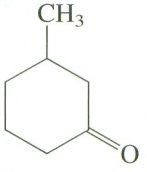
In 2-cyclohexenol, one side of the ring does not mirror the other, so it has no plane of symmetry. It is a chiral molecule.

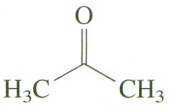
PROBLEM 7.3

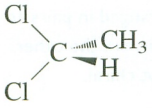
Indicate whether each of these objects or molecules has a plane of symmetry:

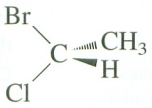
a) Idealized human face **b)** Pencil **c)** Ear

d) 

e) 

f) 

g) 

h) 

7.3 Designating Configuration of Enantiomers

Suppose we are working with one enantiomer of a chiral compound. How can we indicate which enantiomer is being used when writing about it? Or how can we look up the properties of this enantiomer in a reference book? We need a method to designate the configuration of the enantiomer, to denote the three-dimensional arrangement of the four groups around the chirality center, other than drawing the structure. In the case of many everyday chiral objects, the terms *right* and *left* are used, as in a left shoe or right-handed golf clubs. In Section 6.2 we learned how to designate the configuration of geometrical isomers using the Cahn-Ingold-Prelog sequence rules and the labels *Z* and *E*. The method to designate the configuration of enantiomers uses these same rules.

The following steps are used to assign the configuration of a chiral compound:

Step 1

Assign priorities from 1 through 4 to the four groups bonded to the chirality center using the Cahn-Ingold-Prelog sequence rules presented in Section 6.2. The group with the highest priority receives number 1, and the lowest-priority group receives number 4.

Step 2

View the molecule so that the bond from the chirality center to group number 4 is pointed directly away from you. Now determine whether the direction of the cycle proceeding from group 1 to 2 to 3 and back to 1 is clockwise or counterclockwise. If this rotation is clockwise, the configuration is *R* (from the Latin word for right, *rectus*). If the rotation is counterclockwise, the configuration is *S* (from the Latin word for left, *sinister*).

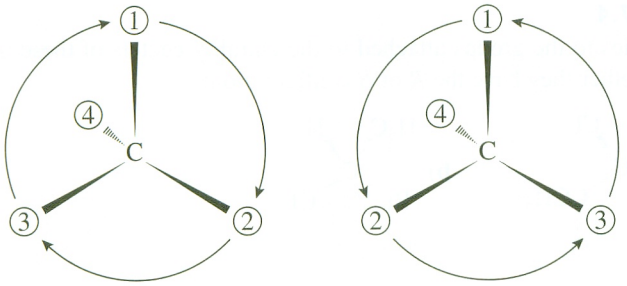
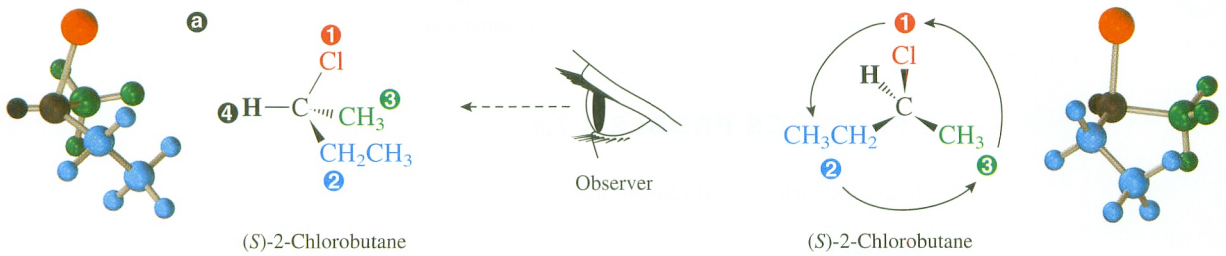


Figure 7.3 gives some examples of how to designate configuration using these rules.

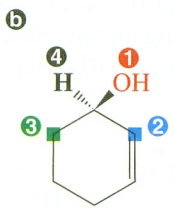
MODEL BUILDING PROBLEM 7.2

Build a model of 2-cyclohexenol with the stereochemistry shown in Figure 7.3 and confirm that it has the *R* configuration.



The group priorities are chlorine = 1, ethyl = 2, methyl = 3, and **hydrogen = 4**. Viewing from the right side, so that the bond from the carbon to the hydrogen is pointed away from the observer, 1 → 2 → 3 → 1 is counterclockwise, so the configuration is S. This is easier to see if the structure is rotated.

In this view, the structure has been rotated so that the bond from the carbon to the hydrogen is pointing directly away from you as you view the page. Now it is easier to see that the direction of 1 → 2 → 3 → 1 is counterclockwise.



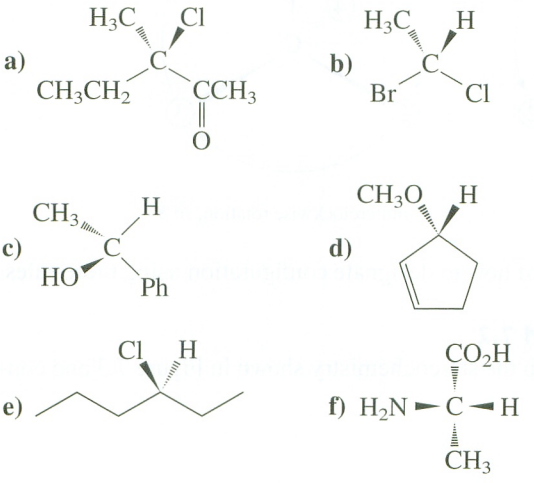
The chirality center is the ring carbon bonded to the OH. The highest-priority group is the OH, and the lowest-priority group is the H. Because the ring carbon on the right of the chirality center is doubly bonded to another carbon, it has higher priority than the other carbon. The lowest-priority group, the hydrogen, is almost pointed directly away from you so the clockwise direction of rotation of 1 → 2 → 3 → 1 can be easily seen.

Active Figure 7.3 ORGANIC Chemistry Now™

DESIGNATING CONFIGURATIONS. a (S)-2-CHLOROBUTANE AND b (R)-2-CYCLOHEXENOL. Test yourself on the concepts in this figure at **OrganicChemistryNow.**

PROBLEM 7.4

Assign priorities to the groups attached to the chirality centers of these molecules and determine whether they have the *R* or *S* configuration:



Alanine
(an amino acid)

PRACTICE PROBLEM 7.1

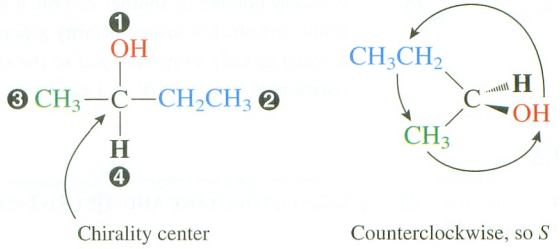
Draw the structure of (*S*)-2-butanol.

Strategy

Draw the structure without stereochemistry, identify the chirality center, and assign priorities to the four groups attached to the chirality center. Then draw a tetrahedral carbon and put the group with the lowest priority on a bond pointed away from you. Put the highest-priority group on any bond. Then put group 2 in the position clockwise from group 1 if it is the (*R*)-enantiomer or in the position counterclockwise from group 1 if it is the (*S*)-enantiomer. Add group 3 to the remaining position.

Solution

The priorities are OH = 1; CH_2CH_3 = 2; CH_3 = 3 ; and H = 4. Put the H on the bond pointed away from you. Put the OH on any bond. Because the (*S*)-enantiomer is desired, put the ethyl group on the bond counterclockwise from the OH group.



Chirality center

Counterclockwise, so *S*

PROBLEM 7.5

Draw structures for these compounds:

a) (*R*)-3-Ethylcyclohexene

b) (*R*)-2-Bromoheptane

ORGANIC Chemistry Now™
Click *Coached Tutorial Problems* to practice using the **Cahn-Ingold-Prelog Sequence Rules.**

The actual three-dimensional arrangement of groups around a chirality center is called the **absolute configuration.** Until a special X-ray technique was developed in 1951, it was impossible to determine the absolute configuration of any compound. Although samples of one enantiomer (or both) of a multitude of compounds were available, no experimental method existed to determine whether that enantiomer had the *R* or the *S* absolute configuration. This was not a major problem for organic chemists, though, because they were able to convert one chiral molecule to another, using reactions whose stereochemical effects were well known. Thus, it was possible to relate the configuration of one compound to that of another. The **relative configurations** of the compounds were known. For example, if one enantiomer of 2-butanol is converted to 2-chlorobutane using a reaction that is known to put the chlorine exactly where the hydroxy group was, then the two compounds have the same relative configuration. If, as shown here, the starting material is (*R*)-2-butanol, then the product is (*R*)-2-chlorobutane:

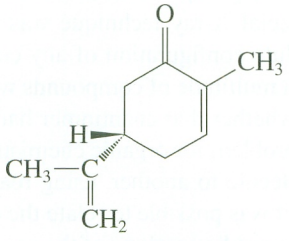
(*R*)-2-Butanol (*R*)-2-Chlorobutane

If the absolute configuration of the starting 2-butanol enantiomer is not known, then the absolute configuration of the product 2-chlorobutane is not known either. However, because the reaction is known to put the chlorine exactly where the hydroxy group was, the two compounds must have the same relative configuration. Often, knowing the relative configurations of the compounds is enough to answer the chemical question under consideration. Of course, once the absolute configuration of one compound has been determined, the absolute configuration of any other compound whose configuration has been related to the first is also known.

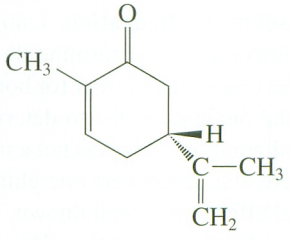
7.4 PROPERTIES OF ENANTIOMERS

When do enantiomers have different properties? Again, it is helpful to draw analogies with everyday objects that are chiral. When do your hands have different properties? They are different when you put on a glove; they are different when you write; they are different when you shake hands. What do these objects or activities have in common? A glove, writing, and shaking hands are all chiral! Hands are different when they interact with one enantiomer of a chiral object or activity. Likewise, enantiomeric molecules are different when they are in a chiral environment. Most commonly, the chiral environment is the presence of one enantiomer of another chiral compound. Otherwise, their properties are identical. For example, the naturally occurring ketones (*R*)- and (*S*)-

carvone have identical melting points, boiling points, solubilities in ethanol, and heats of combustion. However, they have different solubilities in one enantiomer of a chiral solvent, and they have different odors (the odor receptors in the nose are chiral). (*R*)-Carvone smells like caraway and (*S*)-carvone smells like spearmint. An important difference is that *enantiomers have different rates of reaction with one enantiomer of a chiral reagent.*

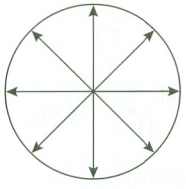


(*S*)-Carvone

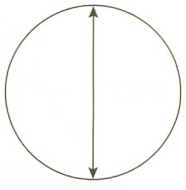


(*R*)-Carvone

The most common method used to detect the presence of chiral molecules in a sample employs the interaction of plane-polarized light with the sample.



Regular light waves consist of electromagnetic fields that oscillate in all directions perpendicular to the direction of travel of the wave. If we could see these fields while viewing the light beam coming directly at us, the oscillations would occur along the arrows.



When a regular light beam is passed through a polarizer (polarized sunglasses will work), all of the light waves, except those whose electromagnetic fields oscillate in a single direction, are filtered out. The result is a beam of **plane-polarized light.** The oscillations all occur in a single plane as shown.

When plane-polarized light is passed through a sample containing one enantiomer of a chiral compound, the plane of polarization of the light is rotated. (Samples that rotate plane-polarized light are said to be **optically active.**) A schematic diagram of a simple instrument, called a polarimeter, that can detect this rotation is shown in Figure 7.4. In this instrument the organic compound to be analyzed is placed in the sample tube, either as a pure liquid or as solution in an achiral solvent. When the plane-polarized light passes through the sample, the plane of polarization is rotated. The magnitude of the observed rotation, α, in degrees, is measured by the analyzing polarizer. If the beam has been rotated in a clockwise direction, α is assigned a positive value; if the beam has been rotated in a counterclockwise direction, α is assigned a negative value.

For a particular compound the observed rotation depends on the concentration of the compound, the path length of the sample tube, and the wavelength of the light that is used. Often the yellow light produced by a sodium lamp, called the sodium D line (wavelength = 589 nm), is used. The specific rotation, a constant characteristic of each

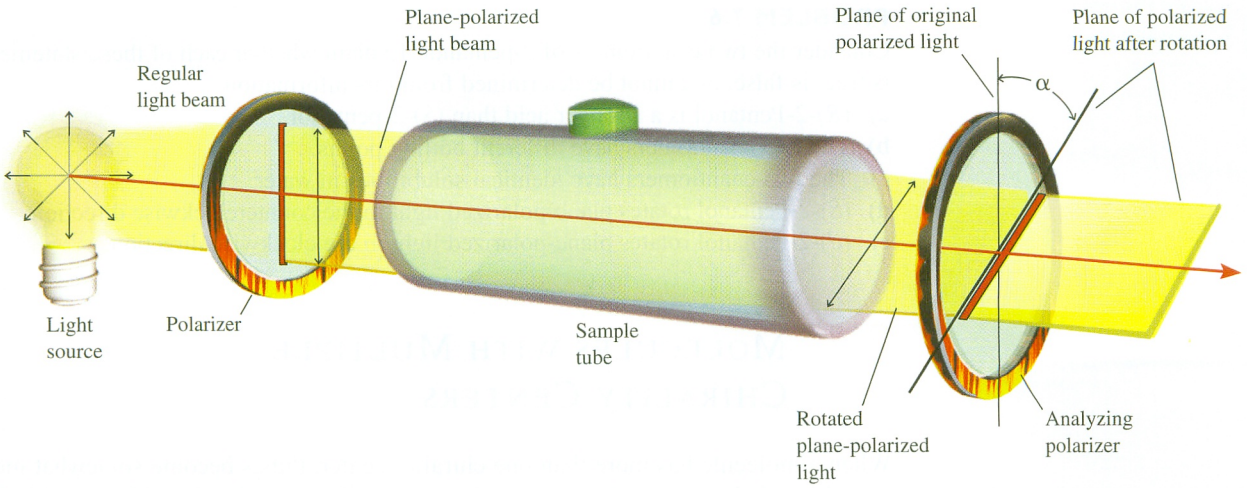


Figure 7.4

SCHEMATIC DIAGRAM OF A POLARIMETER.

chiral compound, can be calculated from the observed rotation obtained in the laboratory by the following equation:

$$[\alpha]_D = \frac{\alpha}{(c)\,(l)}$$

Specific rotation (using sodium D line) — Observed rotation (degrees) — Concentration (g/mL) — Length of sample tube (dm)

Enantiomers rotate plane-polarized light by identical magnitudes but in opposite directions. The enantiomer that rotates the light clockwise is called **dextrorotatory,** (*d*) or (+), while the one that rotates light counterclockwise is called **levorotatory,** (*l*) or (−). A common way to encounter a chiral compound is as an equal mixture of enantiomers, called a **racemic mixture** or a **racemate.** A racemic mixture, often designated as *d,l* or (±), does not rotate plane-polarized light because the rotation due to one enantiomer is canceled by that of the other. Of course, mixtures that have one enantiomer in excess of the other and are neither enantiomerically pure nor completely racemic, may also be encountered.

Methods are available that enable the absolute configuration of some compounds to be predicted from the direction of their rotations, but the process is quite complex. Therefore, the observation that a compound rotates plane-polarized light will indicate to us only that it is chiral and that one enantiomer is present in excess of the other. If the sample contains only one enantiomer, then the specific rotation can be determined. The specific rotation is a constant that can be used to help identify the compound in the same manner as its melting point or boiling point. For example, the specific rotation of sucrose (table sugar) is $[\alpha]_D = +66.37$, and that of (−)-2-butanol is $[\alpha]_D = -13.9$. There is no way for us to tell that the (*l*)-enantiomer of 2-butanol actually has the *R* absolute configuration. In general, there is no relationship between the absolute configuration (*R* or *S*) and the direction of rotation of plane-polarized light (+ or −).

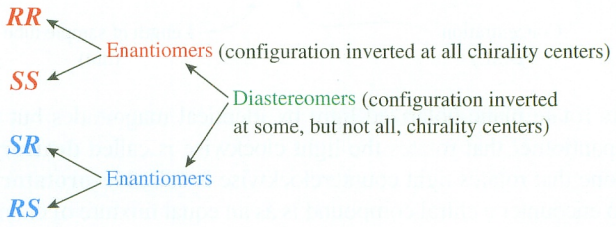
PROBLEM 7.6

Consider the two enantiomers of 2-pentanol. Explain whether each of these statements is true, is false, or cannot be determined from this information.

a) (*R*)-2-Pentanol is a stronger acid than (*S*)-2-pentanol.
b) The two enantiomers have different boiling points.
c) The two enantiomers have identical solubilities in water.
d) (*S*)-2-Pentanol rotates plane-polarized light in the counterclockwise direction.
e) (*d*)-2-Pentanol rotates plane-polarized light in the clockwise direction.

7.5 Molecules with Multiple Chirality Centers

When a molecule has more than one chirality center, things become somewhat more complicated. Let's consider the simplest possibility: a molecule with two chirality centers. Each chirality center can have either the *R* or the *S* absolute configuration. There are four possible combinations: *RR*, *SS*, *RS*, and *SR*. The mirror image of a chiral molecule, that is, its enantiomer, has the opposite configuration (inverted configuration) at all chirality centers. Therefore, the *RR* and the *SS* stereoisomers are enantiomers, as are the *RS* and *SR* stereoisomers. The *RR* and the *RS* stereoisomers are not mirror images. Such non–mirror-image stereoisomers are called **diastereomers.** They have the opposite configuration at some, but not all, chirality centers. (Note that the cis–trans isomers we saw in Chapter 6 are another type of diastereomers.)

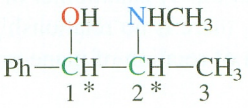


As we saw previously, enantiomers have identical properties unless they are placed in a chiral environment. Diastereomers, on the other hand, are not mirror images and have different properties in all environments. They have different physical properties and different chemical properties.

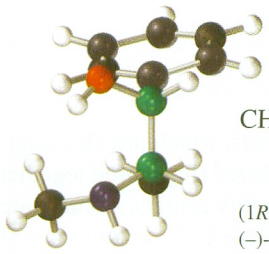
A similar analysis holds for molecules that have more than two chirality centers. Each chirality center may have either the *R* or the *S* configuration. The number of possible stereoisomers can be calculated by using simple probability theory. A molecule with a number of chirality centers equal to *n* has a maximum of 2^n stereoisomers:

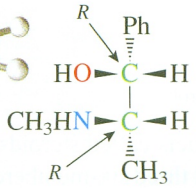
$$\text{maximum number of stereoisomers} = 2^n \qquad (n = \text{number of chirality centers})$$

As an example, consider the case of 2-(methylamino)-1-phenyl-1-propanol:

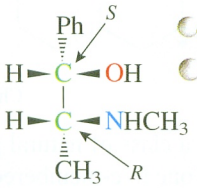


Carbon 1 and carbon 2 are both chirality centers, so there are $2^2 = 4$ stereoisomers. The (1*R*,2*S*)-stereoisomer has a specific rotation of −6.3 and is known as (−)-ephedrine. It is a bronchodilator and is the decongestant used in many cold remedies. It is also the major active ingredient in the herbal supplement ephedra or *ma-huang*. The U.S. Food and Drug Administration has banned the sale of dietary supplements containing ephedra in 2004 because of adverse health effects, including elevated blood pressure and strokes. The enantiomer of (−)-ephedrine, the (1*S*,2*R*)-stereoisomer, does not occur naturally. It has the same melting point as (−)-ephedrine but different physiological properties, and it rotates plane-polarized light in the positive direction. The racemic mixture, (*d,l*)-ephedrine, packs better into a crystal lattice and has a higher melting point (76°C) than either enantiomer.

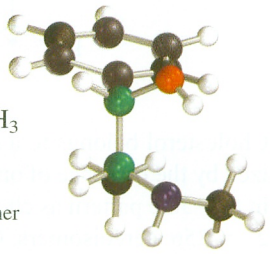




(1*R*,2*S*)-Stereoisomer
(−)-ephedrine
mp: 40°C
$[\alpha]_D$: −6.3

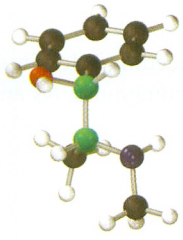


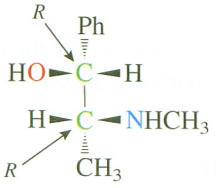
(1*S*,2*R*)-Stereoisomer
(+)-ephedrine
mp: 40°C
$[\alpha]_D$: +6.3



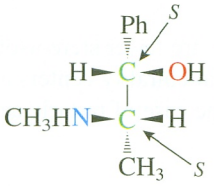
One way to produce a drawing of the enantiomer of (−)-ephedrine is to imagine a mirror placed just to the right of the (−)-ephedrine structure and perpendicular to the page. When the mirror image of the original structure is drawn, the structure on the right, (+)-ephedrine, is produced. Another way to construct the enantiomer is to interchange two groups on each chirality center. (Recall that interchanging any two groups at a chirality center inverts the configuration at that chirality center.) Thus, if the OH and H on carbon 1 of (−)-ephedrine are interchanged and the CH_3NH and H on carbon 2 are interchanged, then the diagram of the enantiomeric (+)-ephedrine on the right is again produced.

To draw a diastereomer of ephedrine, two groups on one chirality center are interchanged, but the configuration at the other chirality center is not changed. For example, if the H and $NHCH_3$ of the preceding diagram of (−)-ephedrine are interchanged, the resulting stereoisomer is the (1*R*,2*R*)-stereoisomer. It is known as (−)-pseudoephedrine, which is used as a nasal decongestant. The two enantiomers of pseudoephedrine have very different physical constants from ephedrine. Their chemical and physiological properties are different also.

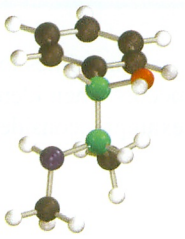




(1*R*,2*R*)-Stereoisomer
(−)-pseudoephedrine
mp: 118°C
$[\alpha]_D$: −52



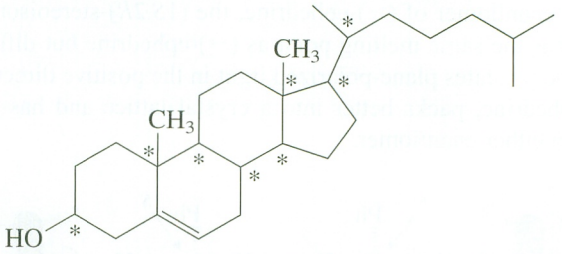
(1*S*,2*S*)-Stereoisomer
(+)-pseudoephedrine
mp: 118°C
$[\alpha]_D$: +52



PROBLEM 7.7

Draw all the stereoisomers of 2-bromo-3-chlorobutane and indicate whether they are enantiomers or diastereomers.

As another example, consider the compound cholesterol:

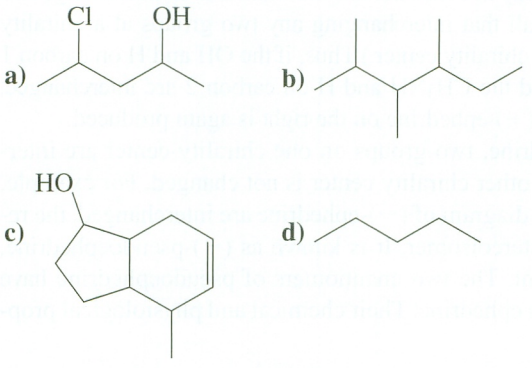


Cholesterol

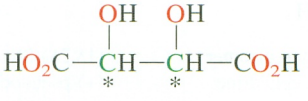
Cholesterol belongs to a class of natural products called steroids, which are characterized by the presence of one five-membered and three six-membered rings fused together in the same pattern as cholesterol. This structure has eight chirality centers, so there are $2^8 = 256$ stereoisomers. Only one of these is cholesterol. Another is the enantiomer of cholesterol, and the other 254 are diastereomers of cholesterol. Of the 256 possibilities, nature produces only one: cholesterol.

PROBLEM 7.8

Label each chirality center in these compounds with an asterisk and calculate the maximum number of stereoisomers for each:

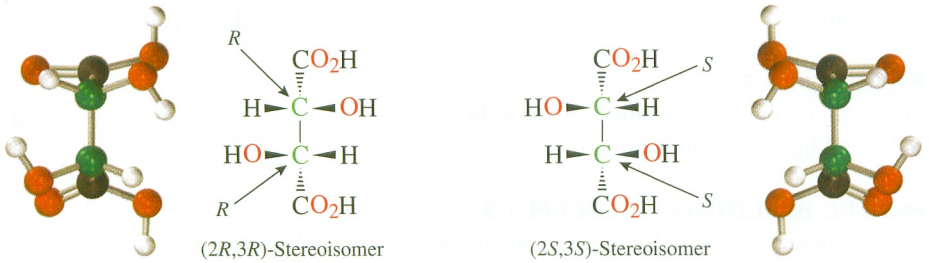


Sometimes there are fewer stereoisomers than predicted by the preceding rule. This occurs when identical chirality centers are symmetrically placed in a compound. As an example, consider the case of tartaric acid.



Tartaric acid

There are two chirality centers, so the formula predicts a total of four stereoisomers. However, each of the chirality centers has identical groups attached to the carbon, so fewer than four stereoisomers actually exist. The analysis can be conducted in the same manner as was done previously for ephedrine. We start by drawing one of the stereoisomers, the (2*R*,3*R*)-isomer for example. Then the mirror image of this, the (2*S*,3*S*)-stereoisomer is drawn. These two compounds are nonsuperimposable mirror images—enantiomers.

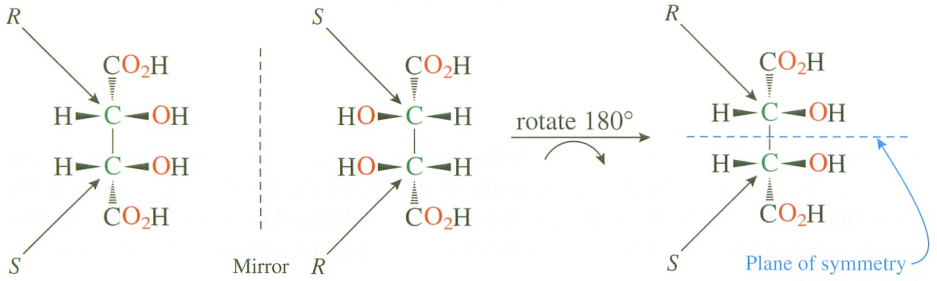


(2*R*,3*R*)-Stereoisomer
(+)-tartaric acid
mp: 169–170°C
$[\alpha]_D$: +12.0

(2*S*,3*S*)-Stereoisomer
(–)-tartaric acid
mp: 169–170°C
$[\alpha]_D$: –12.0

(+)-Tartaric acid occurs naturally in fruits and plants. Its monopotassium salt is called cream of tartar and is a component of baking powder. (−)-Tartaric acid is much less common in nature and has been found only in the fruit of a single West African tree.

A diastereomer of these compounds is constructed by interchanging the H and OH on one of the chirality centers, as shown. The mirror image of this compound is also shown.



(2*R*,3*S*)-Stereoisomer
meso-tartaric acid
mp: 159–160°C

(2*S*,3*R*)-Stereoisomer
meso-tartaric acid
mp: 159–160°C

Careful examination of these mirror images shows that they are, in fact, identical. If the (2*S*,3*R*)-stereoisomer is rotated 180° in the plane of the paper, the structure on the right is produced and it is identical to the (2*R*,3*S*)-stereoisomer on the left. Because the compound is superimposable on its mirror image, it is not chiral and does not rotate plane-polarized light. Another way to determine that this compound is not chiral is to note that it has a plane of symmetry that bisects the C-2—C-3 bond. Compounds such as this one, which contain chirality centers but are not chiral are called ***meso*-stereoisomers.** *meso*-Tartaric acid is human-made and does not occur in nature. Overall, then, tartaric acid has only three stereoisomers: the two enantiomers of the chiral diastereomer (often called the *d,l*-diastereomer) and the *meso*-diastereomer.

Because of its symmetry, numbering can begin at either end of tartaric acid. It is not surprising, then, that (2*R*,3*S*)-tartaric acid is the same as (2*S*,3*R*)-tartaric acid. One of the chirality centers is the mirror image of the other. That is why *meso*-tartaric acid has an internal plane of symmetry. As an everyday example, consider an idealized human figure. Although the figure has chiral parts such as hands and feet, they are present in pairs of left and right enantiomers arranged so that the figure has an internal plane of symmetry. Whenever we encounter a compound that has identical chirality centers, placed symmetrically, we should expect *meso*-stereoisomers to occur, resulting in the total number of stereoisomers being less than that predicted by the 2^n rule.

PROBLEM 7.9

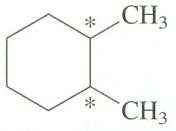
Draw all of the stereoisomers for 2,3-dichlorobutane. Indicate which rotate plane-polarized light and which are meso.

MODEL BUILDING PROBLEM 7.3

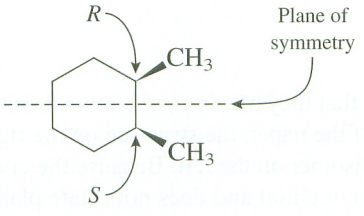
Build a model of *meso*-2,3-dichlorobutane. Build a model of its mirror image. Show that these models superimpose. Locate the plane of symmetry in one of the models.

7.6 Stereoisomers and Cyclic Compounds

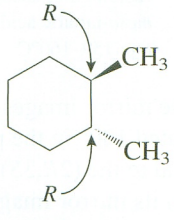
The *cis*- and *trans*-stereoisomers of cyclic compounds that were presented previously are actually just special cases of the type of stereoisomers that we have just discussed. For example, consider the case of 1,2-dimethylcyclohexane:



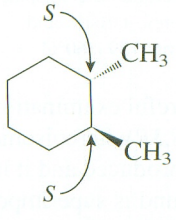
There are two chirality centers, so the formula predicts that there are four stereoisomers. However, because the chirality centers are identical, we expect that there are actually fewer than four stereoisomers. In fact, the analysis is identical to the one we just did for tartaric acid. There are three stereoisomers: a *d,l*-pair of enantiomers and a *meso*-diastereomer.



meso-Stereoisomer
(1*R*,2*S*) or (1*S*,2*R*)
cis-diastereomer



(1*R*,2*R*)-Stereoisomer

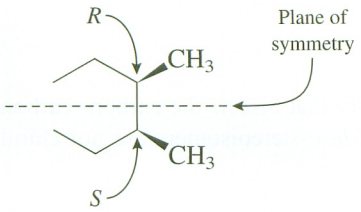


(1*S*,2*S*)-Stereoisomer

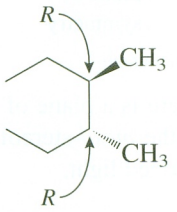
Enantiomers of the *trans*-diastereomer

The *cis*-diastereomer is meso. It has a plane of symmetry bisecting the ring bond between the two methyl groups. It is not chiral and does not rotate plane-polarized light.

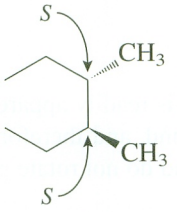
The *trans*-diastereomer exists as a pair of enantiomers. These stereochemical differences do not depend on the presence of the ring. In fact, suppose the ring is cleaved at the C—C bond opposite the one connecting the chirality centers. The resulting compound, 3,4-dimethylhexane, also has three stereoisomers: a *meso*-diastereomer and two enantiomers of a *d,l*-diastereomer. It is just easier to see that the *cis*- and *trans*-diastereomers of 1,2-dimethylcyclohexane are different than it is to see that the *meso*- and *d,l*-diastereomers of 3,4-dimethylhexane are different.



meso-3,4-Dimethylhexane



(3*R*,4*R*)-Dimethylhexane



(3*S*,4*S*)-Dimethylhexane

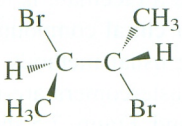
Although cyclohexane rings have chair shapes, rather than being flat, stereochemical analyses such as the preceding one can be done with drawings using planar rings. (This applies to most other rings also.) This is true because the chair conformations are interconverting rapidly and the "average" shape can be considered planar. Careful analysis of one chair conformation of *cis*-1,2-dimethylcyclohexane shows that it is chiral—it is not superimposable on its mirror image. However, the ring-flipped conformation is the enantiomer of the original conformation. Because the conformers interconvert rapidly at room temperature, the compound is not chiral. Again, this result is not unique to ring systems. Some of the conformations of *meso*-3,4-dimethylhexane are also chiral, but there is always an enantiomeric conformation, and interconversion between them is rapid. In looking for internal planes of symmetry in such molecules, it is necessary to use the most symmetrical conformation.

PROBLEM 7.10

Draw all of the stereoisomers of 1,2-dimethylcyclopropane. Explain which rotate plane-polarized light.

PRACTICE PROBLEM 7.2

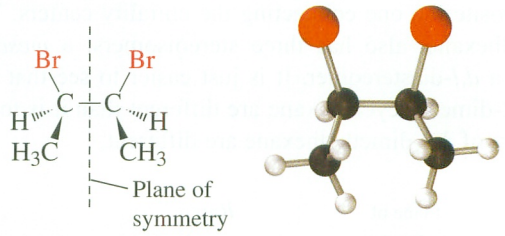
Explain whether this compound would rotate plane-polarized light:



Solution

Because both chirality centers have the same groups attached, this compound might be meso. To determine this, the conformation must be changed to a more symmetrical one

in which at least one pair of like groups is eclipsed. Rotation of the right carbon by 180° gives this conformation.

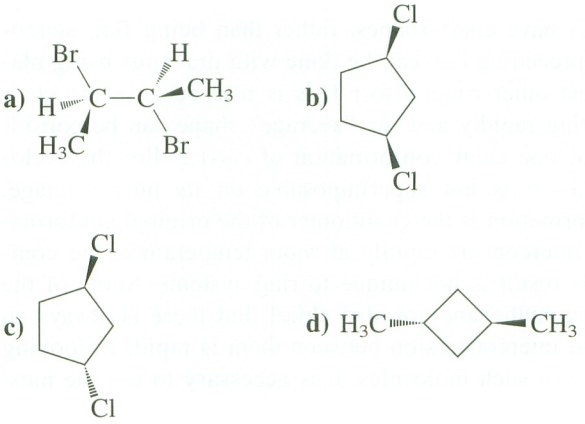


2,3-Dibromobutane

It is readily apparent that there is a plane of symmetry that bisects the carbon–carbon bond, and therefore, this is the *meso*-stereoisomer. *Meso*-stereoisomers are not chiral and do not rotate plane-polarized light.

PROBLEM 7.11

Explain whether these compounds rotate plane-polarized light:



7.7 Resolution: Separating Enantiomers

The process of separating the enantiomers of a racemic mixture is called a **resolution.** To accomplish this task, the environment must be made chiral so that the enantiomers have different properties. These different properties can then be employed in the separation process.

The classical method to resolve a racemate is to react the mixture of enantiomers with one enantiomer of some other chiral compound. The products are diastereomers and can be separated by using the usual methods, such as recrystallization or chromatography. Then the separated diastereomers are individually converted back to the enantiomers of the original compound. Figure 7.5 shows how a racemic carboxylic acid can be resolved.

Another resolution method that is sometimes employed involves the selective reaction of one enantiomer of a racemic mixture with one enantiomer of a chiral reagent,

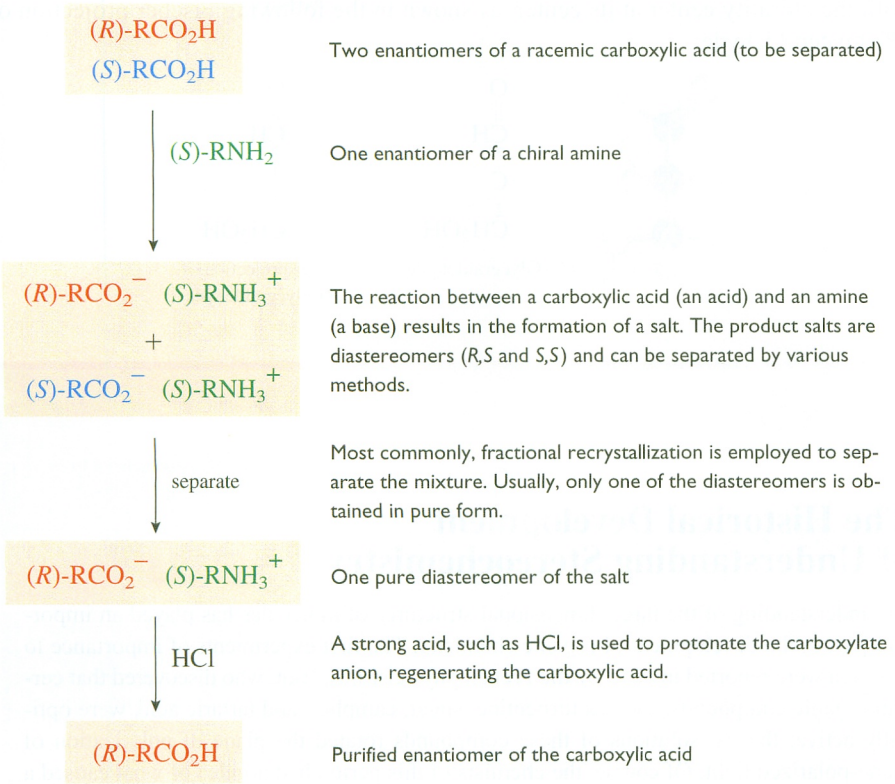

(R)-RCO2H
(S)-RCO2H
Two enantiomers of a racemic carboxylic acid (to be separated)
(S)-RNH2
One enantiomer of a chiral amine
(R)-RCO2− (S)-RNH3+
+
(S)-RCO2− (S)-RNH3+
The reaction between a carboxylic acid (an acid) and an amine (a base) results in the formation of a salt. The product salts are diastereomers (R,S and S,S) and can be separated by various methods.
separate
Most commonly, fractional recrystallization is employed to separate the mixture. Usually, only one of the diastereomers is obtained in pure form.
(R)-RCO2− (S)-RNH3+
One pure diastereomer of the salt
HCl
A strong acid, such as HCl, is used to protonate the carboxylate anion, regenerating the carboxylic acid.
(R)-RCO2H
Purified enantiomer of the carboxylic acid

Figure 7.5

RESOLUTION OF A RACEMIC CARBOXYLIC ACID.

often an enzyme. Either the unreacted enantiomer of the starting material can be isolated or the single enantiomer of the product can be obtained. For example, Louis Pasteur found that fermentation of (±)-tartaric acid with *penicillium glaucum* resulted in the metabolism of the (+)-enantiomer. The unreacted (−)-tartaric acid could be recovered from the fermentation mixture.

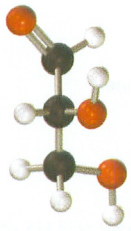
Another method that is becoming very important is chromatography using a chiral phase. Often, a chiral stationary phase, prepared by covalently bonding a chiral compound to the surface of silica beads, is used.

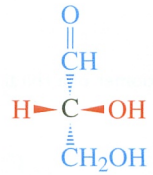
7.8 FISCHER PROJECTIONS

Representing these chiral molecules, especially those with more than one chirality center, using only the two dimensions of a piece of paper, requires some special conventions. We have become accustomed to using wedged and dashed bonds for this purpose. Another method was developed by one of the pioneers in the area of organic stereochemistry, Emil Fischer. To construct a Fischer projection, the molecule is first arranged with the horizontal bonds to its chirality center projecting above the plane of the page and the vertical bonds projecting behind the page. In the Fischer projection the bonds are "projected" into the plane of the page, resulting in a cross

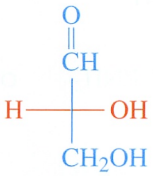
with the chirality center at its center, as shown in the following Fischer projection of (*R*)-glyceraldehyde:

Important Convention





(*R*)-Glyceraldehyde



Fisher projection of (*R*)-glyceraldehyde

Focus On

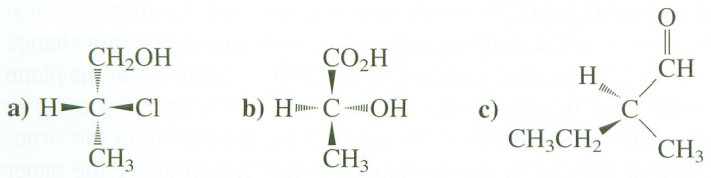
The Historical Development of Understanding Stereochemistry

An understanding of the three-dimensional structures of molecules has played an important part in the development of organic chemistry. The first experiments of importance to this area were reported in 1815 by the French physicist J. B. Biot, who discovered that certain organic compounds, such as turpentine, sugar, camphor, and tartaric acid, were optically active: that is, solutions of these compounds rotated the plane of polarization of plane-polarized light. Of course, the chemists of this period had no idea of what caused a compound to be optically active because atomic theory was just being developed and the concepts of valence and stereochemistry would not be discovered until far in the future.

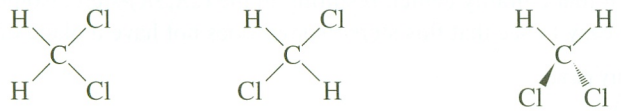
The next major contribution was made in 1848 by the great scientist Louis Pasteur. During the fermentation of wine, large quantities of (+)-tartaric acid precipitate in the barrels. Pasteur was studying a salt of this acid when he discovered that it had a very interesting property. The crystals of this salt had a chiral shape—that is, an individual crystal had a shape that was not superimposable on its mirror image—and all of the crystals had the same handedness. Another tartaric acid, which today is known as racemic tartaric acid, is also produced during the production of wine. It was known that this acid had the same formula as (+)-tartaric acid but was optically inactive, that is, it did not rotate plane-polarized light. Upon careful observation of the salt of this acid, Pasteur found that the individual crystals were chiral, as was the case for (+)-tartaric acid, but in this case the left-handed and the right-handed versions of the crystals were present in equal amounts. Using a tweezers and a magnifying glass (and considerable patience), Pasteur was able to separate these crystals. He found one to be completely identical to the salt of (+)-tartaric acid that he had studied previously. The other had identical physical and chemical properties except that it rotated plane-polarized light in the opposite direction. Pasteur had accomplished the first resolution of a racemic organic compound! Because the salts that gave mirror-image crystals also gave opposite rotations, Pasteur associated optical rotation with chirality. And because solutions of these salts were optically active, he proposed that chirality was not just a macroscopic property of the crystals, but the arrangement of the atoms in a molecule of tartaric acid must also be chiral. He was postulating a chiral shape for the arrangement of these atoms at about the same time that Kekulé was proposing the concept of valence!

PROBLEM 7.12

Draw Fischer projections for these compounds:



It took about another 20 years for the explanation of chirality to be completed. In 1874, two young chemists, Jacobus van't Hoff from Holland and Joseph Le Bel from France, independently proposed that the four bonds to a carbon were arranged in a tetrahedral manner. Their arguments were based on the number of isomers that exist for various formulas. Although we will not go into all of the details here, the following discussion presents some of the reasoning they used. At the time, it was well accepted that all four of the bonds to a carbon were identical. This was based on the fact that, for a multitude of compounds with the formula CH_3X, only one isomer had ever been found. There is only one CH_3Cl, one CH_3OH, one CH_3CH_3, and so on. Many geometries with low symmetries can be eliminated on the basis of this observation. Two arrangements of the four bonds around a carbon that meet the criterion of having all of the bonds identical are the one with a square planar geometry and the one with a tetrahedral geometry. The square planar geometry can be eliminated on the basis of the observation that, for a multitude of compounds with the formula CH_2X_2, only one isomer has ever been found. There is only one CH_2Cl_2. If carbon had a square planar geometry, then two isomeric compounds with the formula CH_2Cl_2 would be expected, as shown here. However, a tetrahedral geometry predicts only one CH_2Cl_2.

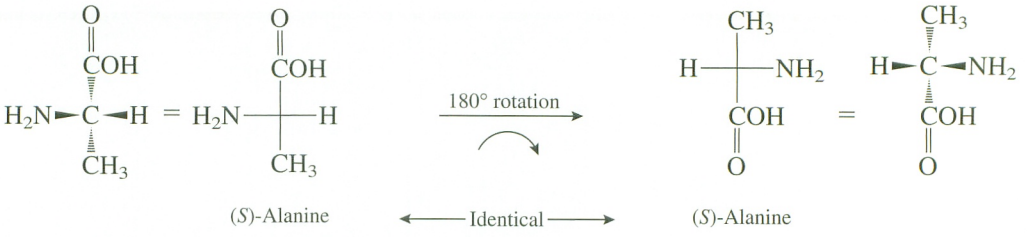


Two isomers with square planar geometry

One isomer with tetrahedral geometry

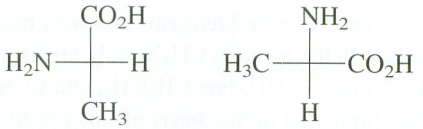
At the time of van't Hoff's and Le Bel's work, there were only a few optically active compounds whose structures had been determined. All of these compounds had a carbon bonded to four different groups, a carbon that we today call a chirality center. van't Hoff and Le Bel pointed out that a tetrahedral arrangement of four different groups around a carbon produced a structure that is not superimposable on its mirror image, a chiral structure. Thus, their postulate of a tetrahedral carbon explained the existence of enantiomeric compounds.

Because they are two-dimensional representations of three-dimensional objects, extreme care must be used in manipulating Fischer projections to avoid changing the configuration. Structures may not be "lifted" out of the plane of the paper. A 180° rotation *in the plane* is permitted, but 90° and 270° rotations are not allowed. As illustrated next for (*S*)-alanine, a 180° rotation of the drawing in the plane of the paper does not change the configuration. A 90° or 270° rotation in the plane or a 180° rotation out of the plane all result in a representation of the enantiomer of the original structure. If you are in doubt, it is always advisable to draw the three-dimensional representation for the structure before manipulating it. Remember that horizontal bonds project above the paper and vertical bonds project behind the paper.

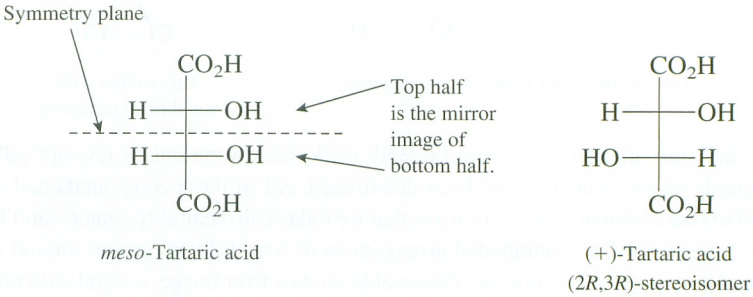


MODEL BUILDING PROBLEM 7.4

Build models of the compounds represented by these Fischer projections. Determine whether the models superimpose. (Note that these Fischer projections are related by a 90° rotation in the plane of the page.)

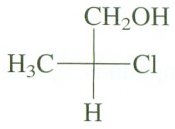


Fischer projections are especially useful in the case of compounds with more than one chirality center. For example, it is easy to see the plane of symmetry in *meso*-tartaric acid. As was the case with regular structures, interchanging any two groups in a Fischer projection results in inversion of configuration at the chirality center. Thus, interchanging the H and OH on the lower chirality center of *meso*-tartaric acid inverts the configuration at that chirality center, resulting in the (2*R*,3*R*)-stereoisomer, (+)-tartaric acid. It is also easy to see that this stereoisomer does not have a plane of symmetry.



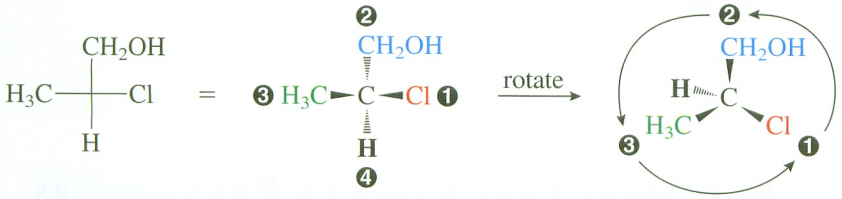
PRACTICE PROBLEM 7.3

Assign the configuration of this compound as *R* or *S*:



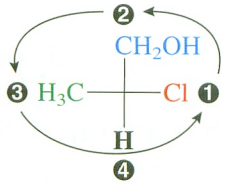
Solution

One way to work this type of problem is to draw the structure, showing its stereochemistry, and then proceed as in previous examples.



S

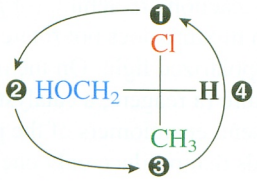
The configuration can also be assigned directly from the Fischer projection. First assign priorities to the groups:



S

If group 4 is attached to a vertical bond, as in this case, it is already pointed away from you. Therefore, the direction of rotation given by proceeding from group 1 to 2 to 3 gives the configuration directly. In this case the rotation is counterclockwise, so the configuration is *S*.

If group 4 is attached to a horizontal bond, it is pointed toward you and you are viewing the molecule from the wrong side.



R

This simply means that the configuration is opposite that given by the direction of rotation proceeding from group 1 to 2 to 3. In this example the direction of rotation is counterclockwise but the H is pointed toward you, so the configuration is *R*. (Try drawing the stereochemistry to confirm this.)

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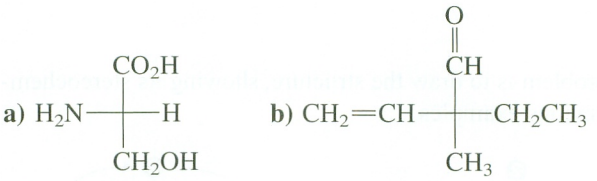
Click *Coached Tutorial Problems* for more practice using **Fischer Projections.**

PROBLEM 7.13

Assign the configurations of the compounds represented by these Fischer projections as *R* or *S*.

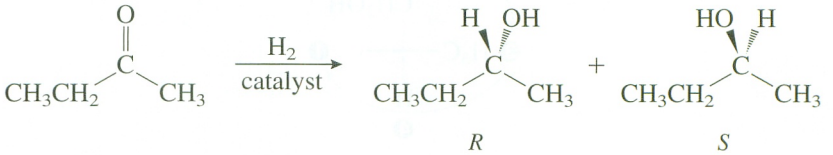
BioLink



Serine

7.9 Reactions That Produce Enantiomers

A reaction of an achiral molecule may introduce a chirality center, producing a chiral product. For example, reaction of the following ketone with hydrogen in the presence of a catalyst results in addition of the hydrogen to the carbon–oxygen double bond, producing 2-butanol:



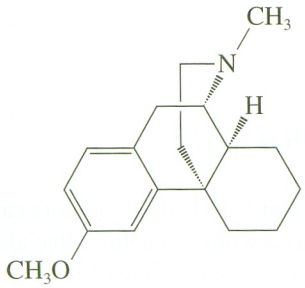
2-Butanone — *R* — *S* — 2-Butanol

The starting ketone is not chiral, but the product alcohol is chiral. Approach of the hydrogen from above the plane of the ketone (as drawn) produces (*R*)-2-butanol, whereas approach from behind the plane produces (*S*)-2-butanol. There is no apparent reason why the hydrogen should prefer one approach over the other; in fact, the two enantiomers are produced in exactly equal amounts—the product is racemic. As long as there is nothing else that is chiral in the reaction, the enantiomeric products (and the enantiomeric reaction pathways leading to them) have identical energies and must be produced in equal amounts. If all the reagents in a reaction are achiral (or racemic), then the product must be racemic. If the initial reaction mixture does not rotate plane-polarized light, the product mixture cannot rotate plane-polarized light. On the other hand, if one of the components of the initial reaction mixture (a reagent, a catalyst, even the solvent) is chiral and only one enantiomer of it is present, enantiomers of the product may be produced in unequal amounts. Devising methods that produce only one enantiomer of a chiral product, called asymmetric synthesis, is one of the most challenging areas of research facing organic chemists today.

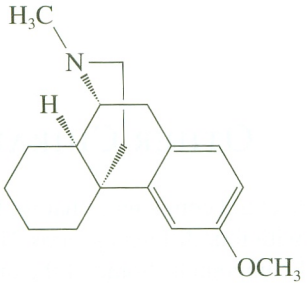
Focus On

Pharmaceuticals and Chirality

Many of the drugs that are so important in medicine today contain chirality centers. If the drug is isolated from a natural source, it is usually obtained as a single enantiomer. But synthetic drugs have most commonly been used as a racemic mixture because obtaining them as single enantiomers is often a time-consuming and expensive process. Because biological processes involve chiral molecules, the effect of drug enantiomers is often different. For example, dextromethorphan is a cough suppressant used in medications such as Robitussin. Its enantiomer, levomethorphan, is a powerful narcotic.

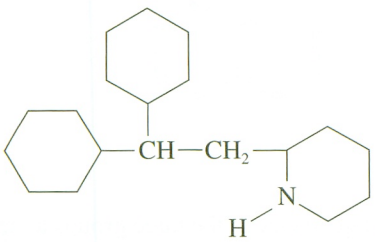


Dextromethorphan

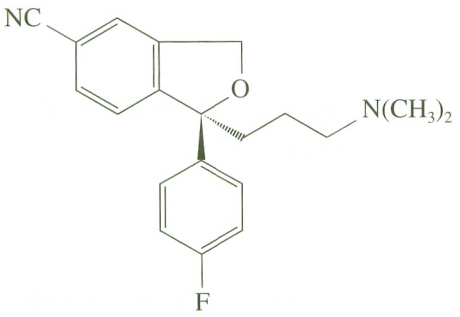


Levomethorphan

If a drug is used as a racemic mixture, often only one of the enantiomers is responsible for the desired pharmacological effect. The other enantiomer may have a lesser effect, or no effect, or may even be responsible for undesired side effects. One example is perhexiline, a racemic drug that was used to treat abnormal heart rhythms. This drug was responsible for a number of deaths in the 1980s because one enantiomer was metabolized much more slowly than the other and accumulated at toxic levels. If perhexiline had been marketed only as the more rapidly metabolized enantiomer, it *might* have been a safer drug.



Perhexiline



(*S*)-Citalopram

Continued

An example of improved efficacy of an enantiomerically pure version of a drug over the racemic version is provided by citalopram. The racemic version, known as Celexa, is marketed as an antidepressant. Studies on the resolved enantiomers have shown that the S-enantiomer is the active one and that it has a more rapid onset of action and a more favorable benefit-to-risk ratio than the racemate. As a result, (S)-citalopram (escitalopram or Lexapro) is now being marketed. Not only is this a better and safer drug, but the pharmaceutical company that developed citalopram was able to extend its market exclusivity for an additional 3 years.

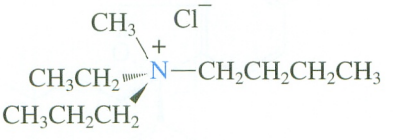
Sales of single enantiomer drugs exceeded $159 billion in 2002. Some of these come from biological sources, but the majority are synthetic. For this reason, the development of synthetic methods that produce only a single enantiomer of chiral compounds is a very active research area in both academic and pharmaceutical research labs. Chiral or asymmetric syntheses, which produce only the desired enantiomer, are much preferred over resolution processes, in which at least half of the initial compound is discarded.

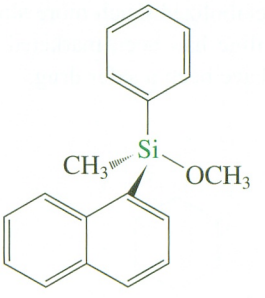
7.10 Other Chiral Compounds

All of the chiral compounds that we have seen so far have had one or more carbons substituted with four different groups. However, there are other situations that also give rise to chiral compounds. Some of the other possibilities are described here.

Other Tetrahedral Atoms

Of course, any tetrahedral atom, not just carbon, that has four different groups bonded to it is a chirality center, and compounds containing such atoms will exist as a pair of enantiomers. Many such compounds have been prepared and resolved, including the following quaternary ammonium salt and the silicon compound:

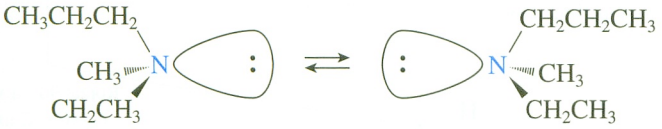




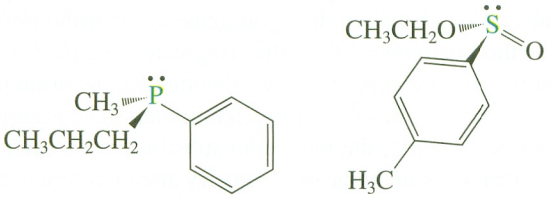
Pyramidal Atoms

A nitrogen with three single bonds has pyramidal geometry. If the three groups attached to the nitrogen are different, then the nitrogen is a stereocenter and the compound exists as a pair of enantiomers. The situation is very similar to a tetrahedral carbon, but with the unshared pair of electrons replacing one of the bonds. However, because there

are only three bonds, the groups can move to the other side of the nitrogen in a process reminiscent of an umbrella turning inside out. This results in inversion of configuration. The activation barrier is quite small, only about 5 kcal/mol (21 kJ/mol). Therefore, inversion is quite fast at ambient temperatures, occurring about 10^{11} times per second. Because the two enantiomers interconvert so rapidly, they cannot be separated. The compound behaves as a racemate, and the existence of the rapidly inverting enantiomeric forms can be ignored.

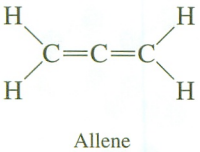


However, compounds containing other pyramidal atoms, with larger barriers to inversion, can be resolved. Examples include the following phosphorus compound (inversion barrier of about 30 kcal/mol [126 kJ/mol]) and the sulfur compound (inversion barrier of about 35 kcal/mol [146 kJ/mol]):

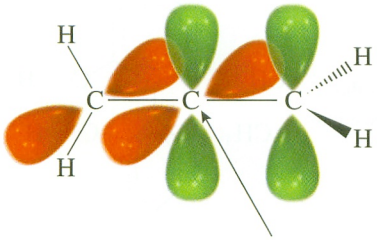


Substituted Allenes

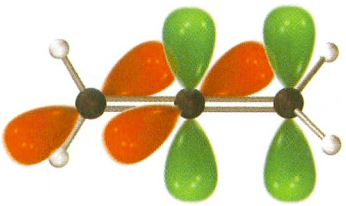
Allene has two adjacent carbon–carbon double bonds. Its geometry is not planar like a normal alkene. The central carbon is *sp* hybridized and has linear geometry. The two *p* orbitals that it uses for the two double bonds are perpendicular, so the planes of the two double bonds are perpendicular. The two hydrogens on one end of allene lie in a plane perpendicular to the two hydrogens on the other end.



Allene

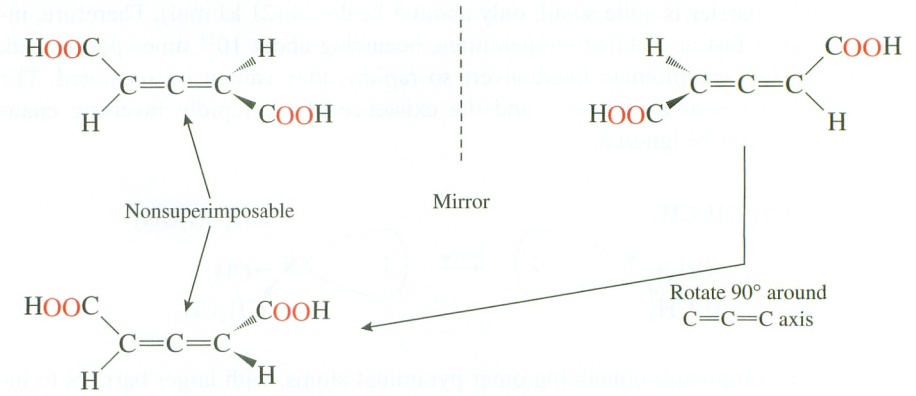


sp Hybridized



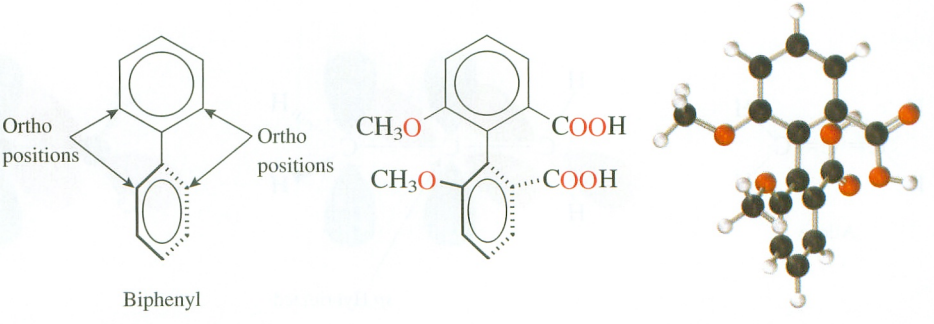
As early as 1875, van't Hoff pointed out that properly substituted allenes would be chiral. When the two groups on one end of the allene are different and the two groups on the other end of the allene are also different, the compound is chiral and exists as a pair of enantiomers, rather than as cis–trans isomers as is the case with simple alkenes.

A number of chiral allenes, such as the following dicarboxylic acid, have been prepared and resolved.



Biphenyls

The compound formed by connecting two benzene rings by a single bond is called biphenyl. Steric interactions between the hydrogens on the ortho positions of one ring with those on the ortho positions of the other ring cause the planes of the rings to be perpendicular. If both rings are appropriately substituted at the ortho positions, then the compound is chiral and can be resolved into enantiomers. The groups in the ortho positions serve two purposes. First, the two ortho substituents on each ring must be different so that the biphenyl has no plane of symmetry and therefore is chiral. In addition, because rotation about the single bond connecting the rings (a conformational change) interconverts the enantiomers, the ortho groups must be large enough that their steric interaction raises the energy barrier for this conformational change. If the groups are large enough, rotation is slow at ambient temperatures, and the compound can be resolved. For example, the enantiomers of the following substituted biphenyl do not interconvert at room temperature, and the compound has been resolved. Rotation about the connecting single bond does occur at higher temperatures. The half-life for racemization is 78 min at 118°C.

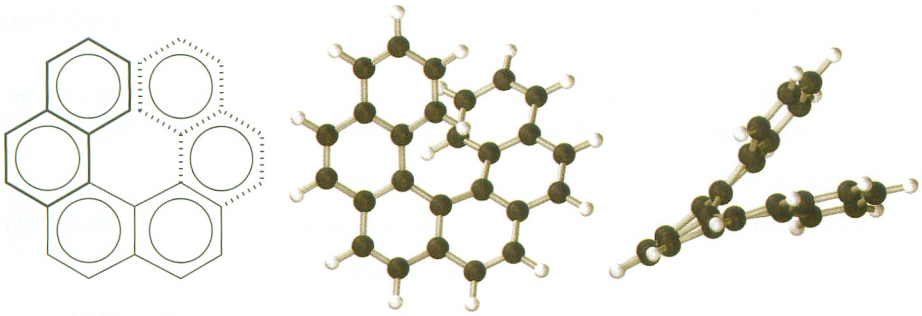


Biphenyl

Helical Molecules

Another interesting group of chiral compounds results when molecules are forced to adopt a helical geometry. Like the turn of a screw, the turn of the helix can be either right-handed or left-handed. One example is the compound known as hexahelicene, which has six aromatic rings fused together. The molecule is forced to adopt a helical

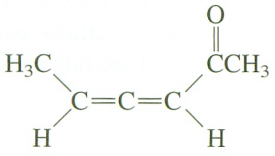
shape to avoid a severe steric interaction between the end rings. Hexahelicene has been resolved and has an enormous specific rotation of +3640.

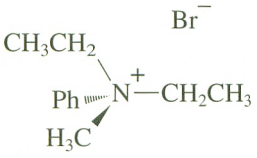


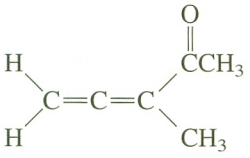
Hexahelicene Top view Side view

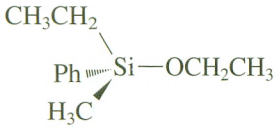
PROBLEM 7.14

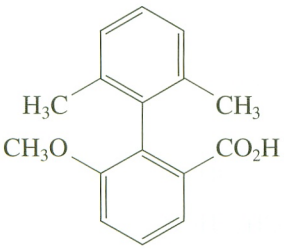
Explain whether each of these compounds is chiral or not:

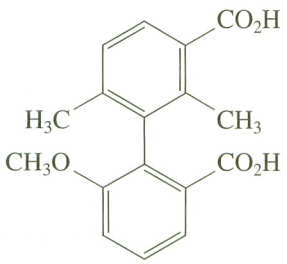
a) 

b) 

c) 

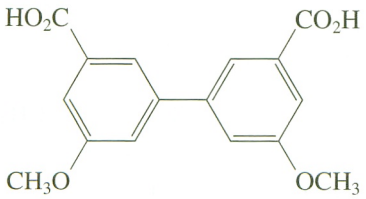
d) 

e) 

f) 

PROBLEM 7.15

Although this biphenyl is chiral, it cannot be resolved. Explain.



Review of Mastery Goals

After completing this chapter, you should be able to:

- Identify chiral compounds, locate chirality centers, and determine how many stereoisomers exist for a particular compound. (Problems 7.18, 7.19, 7.22, 7.27, and 7.29)
- Locate any symmetry planes that are present in a molecule. (Problem 7.20)

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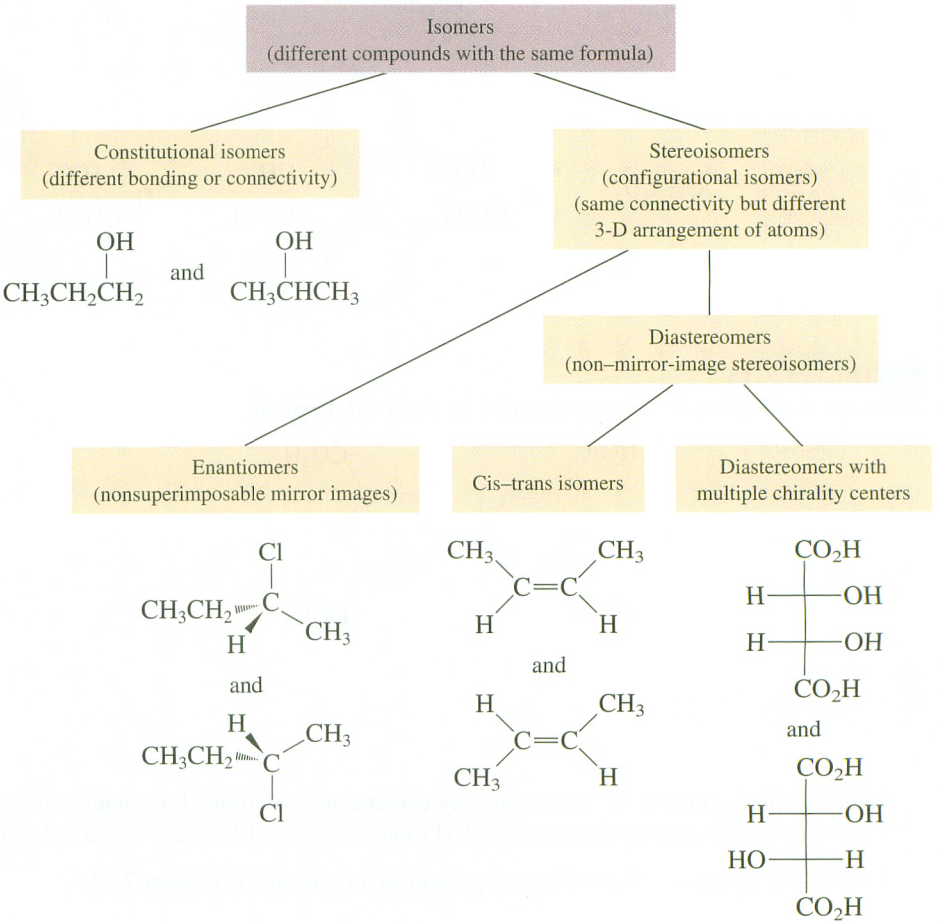
Click *Mastery Goal Quiz* to test how well you have met these goals.

- Designate the configuration of chirality centers as *R* or *S*. (Problems 7.16, 7.17, and 7.30)
- Recognize the circumstances under which enantiomers have different properties. (Problem 7.21)
- Understand when a compound, mixture, or solution is optically active and what information this provides about the sample. (Problems 7.20, 7.21, and 7.24)
- Recognize *meso*-stereoisomers. (Problems 7.20 and 7.28)
- Understand the principles behind the process of separating enantiomers. (Problem 7.25)
- Be able to use Fischer projections properly. (Problem 7.23)
- Identify other chiral molecules, such as biphenyls and allenes. (Problem 7.31)

Visual Summary of Isomers

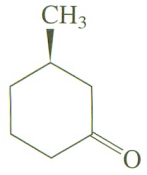
The following scheme summarizes the types of isomers that we have encountered. (Because the rotations about sigma bonds that interconvert conformations occur rapidly at room temperature, conformations cannot be separated and are not considered to be isomers.)



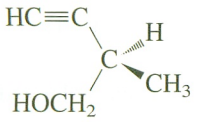
Additional Problems

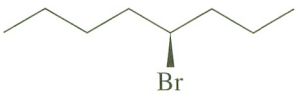
ORGANIC Chemistry Now™
Assess your understanding of this chapter's topics with additional quizzing and conceptual-based problems at **http://now.brookscole.com/hornback2**

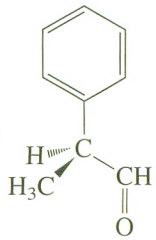
7.16 Assign the configuration of these compounds as *R* or *S*:

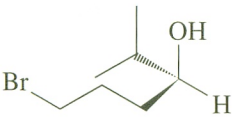
a) 

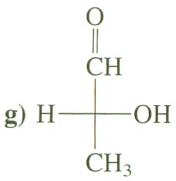
b)

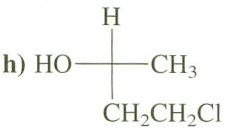
c) 

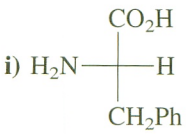
d) 

e) 

f) 

g) 

h) 

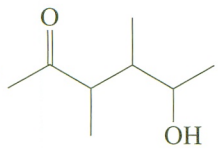
i) 

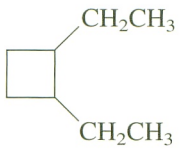
Phenylalanine

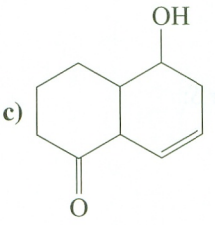
BioLink

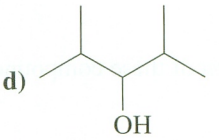
7.17 Draw the structures of these compounds:
a) (*R*)-3-Chloro-1-pentene
b) (*S*)-1-Methyl-2-cyclohexenol

7.18 Determine the number of stereoisomers for these compounds:

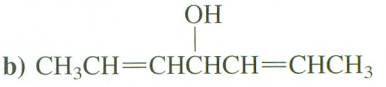
a) 

b) 

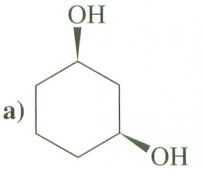


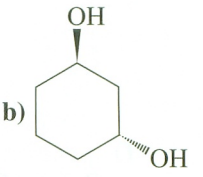


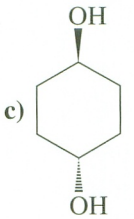
7.19 Draw all of the stereoisomers of these compounds:

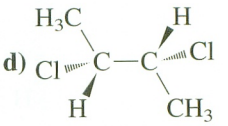


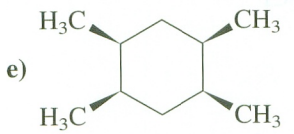
7.20 Explain whether or not these compounds would rotate plane-polarized light:

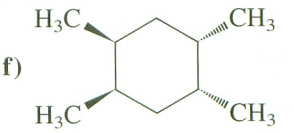


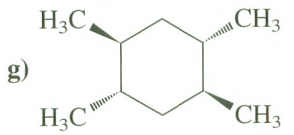


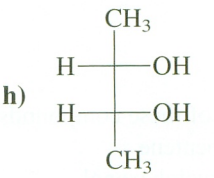


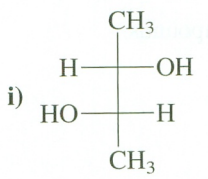




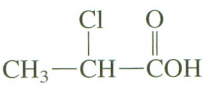






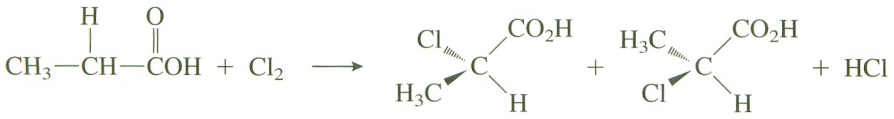


7.21 Consider the two enantiomers of this carboxylic acid:

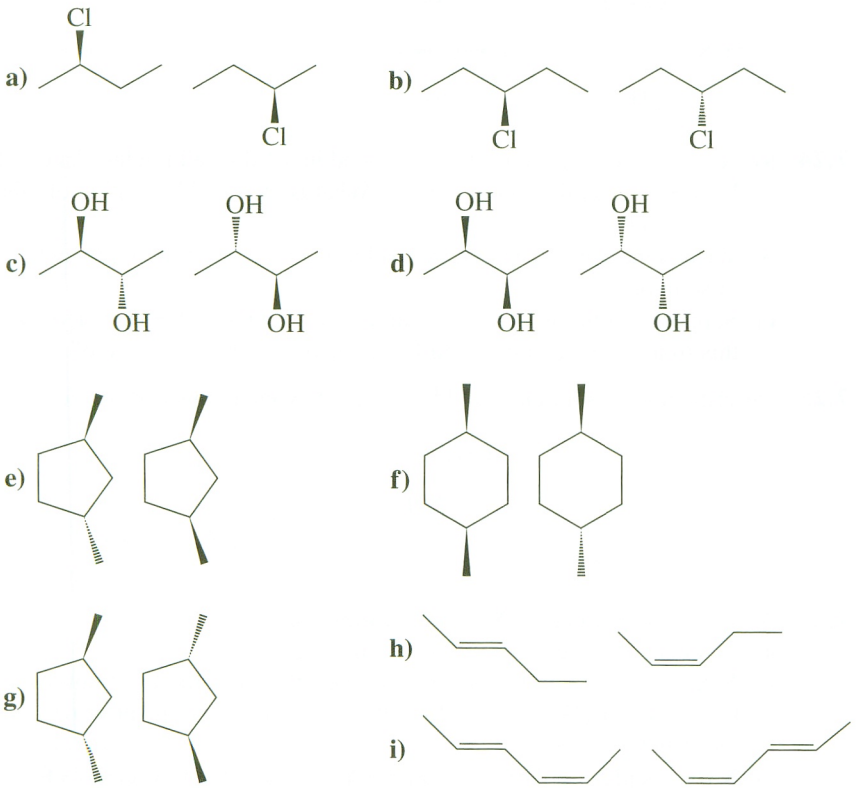


Explain whether each of the following statements is true, is false, or cannot be determined from this information:

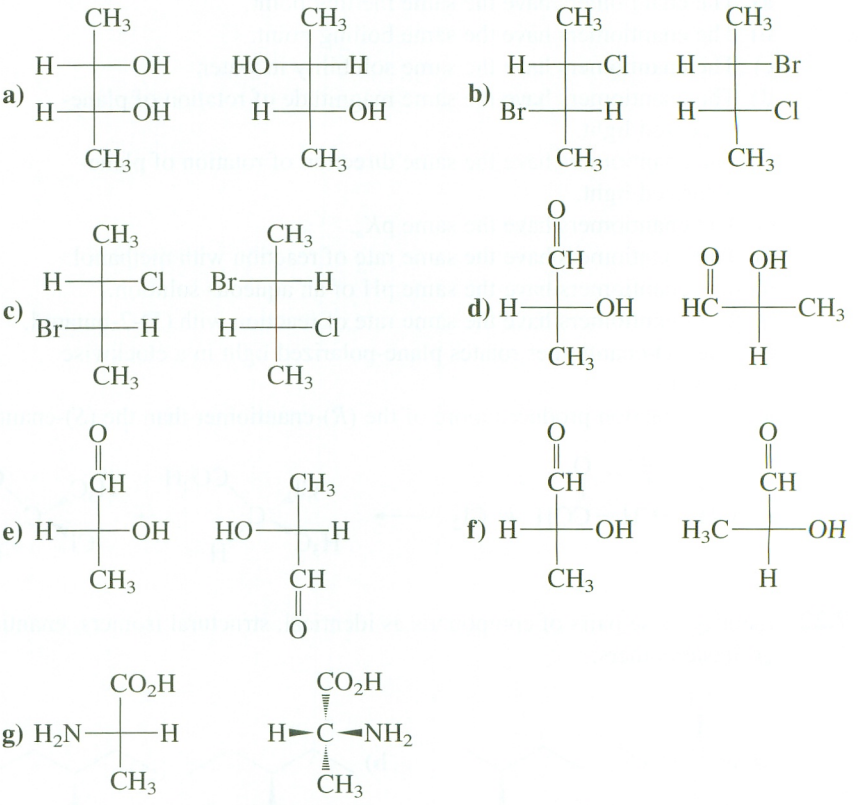
a) The enantiomers have the same melting point.
b) The enantiomers have the same boiling point.
c) The enantiomers have the same solubility in water.
d) The enantiomers have the same magnitude of rotation of plane-polarized light.
e) The enantiomers have the same direction of rotation of plane-polarized light.
f) The enantiomers have the same pK_a.
g) The enantiomers have the same rate of reaction with methanol.
h) The enantiomers have the same pH of an aqueous solution.
i) The enantiomers have the same rate of reaction with (*S*)-2-butanol.
j) The (*R*)-enantiomer rotates plane-polarized light in a clockwise direction.
k) This reaction produces more of the (*R*)-enantiomer than the (*S*)-enantiomer.



7.22 Identify these pairs of compounds as identical, structural isomers, enantiomers, or diastereomers:



7.23 Identify these pairs of compounds as identical, structural isomers, enantiomers, or diastereomers:

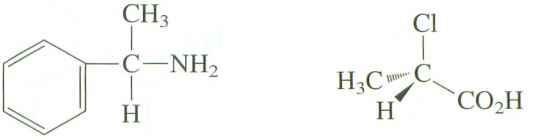


7.24 **a)** A solution of 0.2 g/mL of a compound in a 1 dm cell rotates plane-polarized light +13.3° at the sodium D line. What is the specific rotation of this compound?

b) What is the rotation caused by a solution of 0.1 g of this compound in 10 mL of solution?

c) Suppose a solution of a compound gave a rotation of +160°. How could this rotation be distinguished from one of −200°? from one of +520°?

7.25 Describe how this amine could be resolved by using this carboxylic acid:



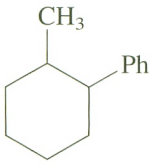
7.26 An unknown compound, **X,** has the formula C_6H_{12}.

a) Calculate the degree of unsaturation of **X.**

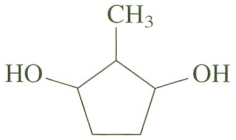
b) **X** reacts with H_2 in the presence of a catalyst to form a compound, **Y,** with the formula C_6H_{14}. What information does this experiment provide about the structure of **X**?

c) **X** rotates plane-polarized light, but **Y** does not. Show structures for **X** and **Y.**

7.27 How many stereoisomers exist for this compound? Assign the relative stabilities of each. Is the methyl group axial or equatorial in the more stable conformer of the least stable stereoisomer?



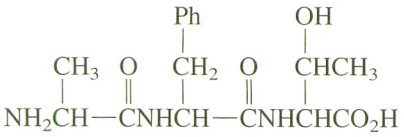
7.28 Draw a stereoisomer of this compound that is chiral, and draw two that are not chiral:



7.29 Many compounds are found as a single stereoisomer in nature even though they have numerous chirality centers. Determine how many chirality centers are present in each of the following naturally occurring compounds and how many stereoisomers are possible for each:

BioLink

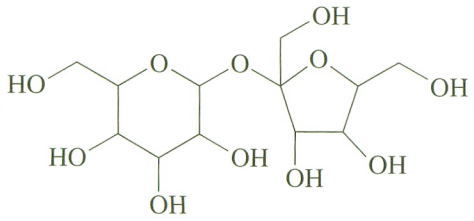
a)



Alanine residue — Phenylalanine residue — Threonine residue

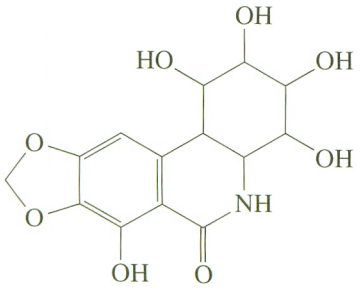
(a tripeptide)

b)



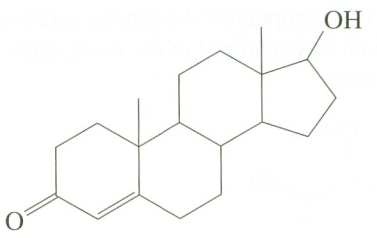
Sucrose
(table sugar)

c)



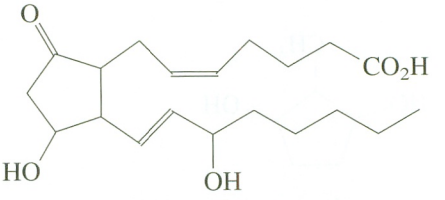
Pancratistatin
(an anticancer drug)

d)



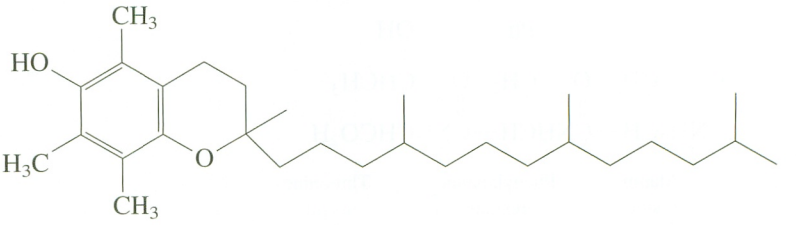
Testosterone
(a steroidal hormone)

e)



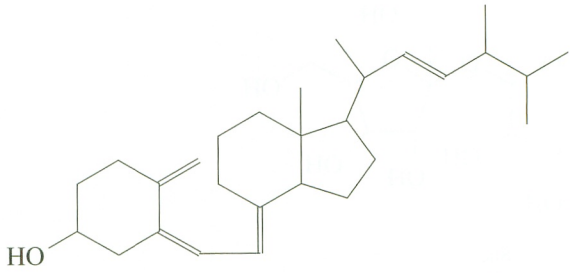
PGE_2
(a prostaglandin)

f)



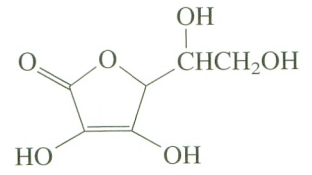
Vitamin E

g)



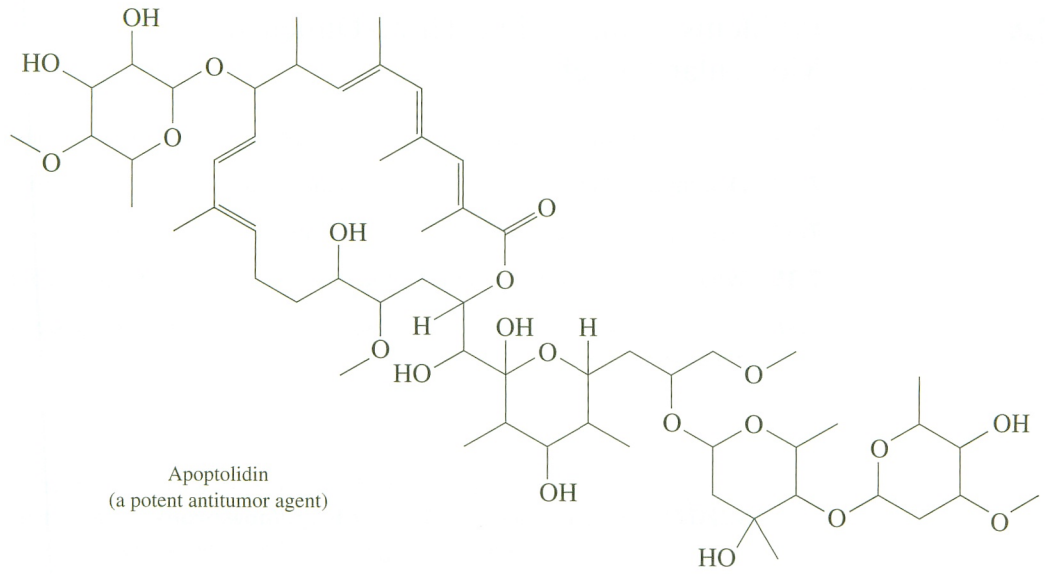
Vitamin D_2

h)



Ascorbic acid
(vitamin C)

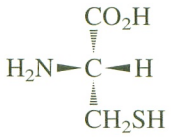
i)



Apoptolidin
(a potent antitumor agent)

7.30 All naturally occurring amino acids have the same relative configuration. All have the *S* absolute configuration, except for cysteine, which has the *R* configuration. Explain.

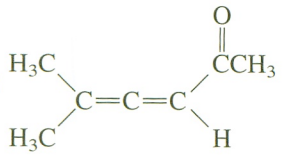
BioLink



Cysteine

7.31 Explain whether each of these compounds is chiral or not:

a)



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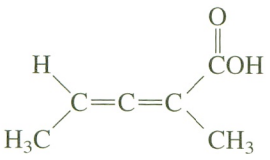
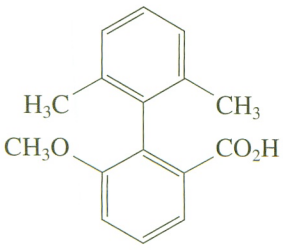
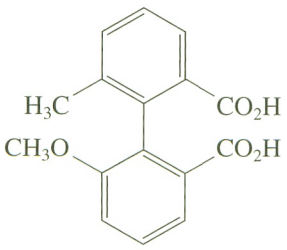


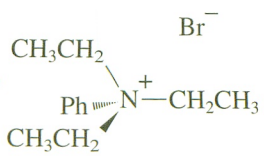
c)



d)



e)



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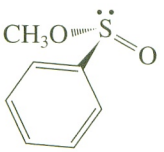

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7.32 Indicate whether these compounds are identical, enantiomers, or diastereomers.

7.33 Determine whether each of the compounds is the *R* or the *S* enantiomer.

7.34 Determine whether each of these compounds is chiral or not.

7.35 What is the relationship between the model and the Fischer projection?

7.36 How many chirality centers are present in estradiol? How many stereoisomers does estradiol have?

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